EXAMINER'S AMENDMENT AND COMMENTS

1. The response and Amendment filed 19 August 2008 to Office Action mailed 01 July 2008 is acknowledged and entered.

2. Also acknowledged is the Declaration from Dr. Anirban Maitra under 37 C.F.R. §1.132 filed 19 August 2008.

Withdrawal of Rejections based on Applicant's Amendments

3. In consideration of remarks, amendments and Declaration from Dr. Anirban Maitra under 37 C.F.R. §1.132 filed 19 August 2008, following objections/rejections in Office Action mailed 01 July 2008 are hereby withdrawn:

- Objection to each of Claims 9-10, 15-16 and 40 for lack of a comma (i.e., ",") at Line 1of each of said claims;
- Rejection to Claims 1-4, 9-12, 14-17 and 40-41 for lack of written description requirement under 35 U.S.C. §112, 2nd paragraph; and
- Indefiniteness rejection to Claims 15 and 40-41 under 35 U.S.C. §112, 2nd paragraph.

Claims Status

4. Claims 5-8, 13 and 18-39 remain cancelled.

5. Claims 1, 9-10, 15-16 and 40-41 have currently been amended.

6. Claims 1-4, 9-12, 14-17 and 40-41 are currently pending and are examined on merits.

Examiner's Amendment

7. An Examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicants, an amendment may be filed as provided by 37 C.F.R. §1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this Examiner's amendment was given in a telephone interview on 10 November 2008 with Mr. Paul M.Booth, Applicants' Representative.

In the Claims:

The following listing of claims will replace all prior versions, and listings, of claims in the instant application:

1. (Currently amended) A method of preparing a biomolecule lysate, comprising the steps of:

(a) heating a composition comprising a formalin fixed biological sample and a reaction buffer at a temperature ~~between about~~ **from** 80°C **to** ~~and about~~ 100°C for a period of time from ~~about~~ 10 minutes to ~~about~~ 4 hours to reverse or release protein cross-linking in said biological sample, and

(b) treating the resulting composition with an effective amount of a proteolytic enzyme selected from the group consisting of trypsin, chymotrypsin, and endoproteinase Lys-C for a period of time from ~~about~~ 30 minutes to ~~about~~ 24 hours at a temperature ~~between about~~ **from** 37°C to ~~about~~ 65°C to disrupt the tissue and cellular structure of said biological sample and to liquefy said sample, thereby producing a liquid, soluble, dilutable biomolecule lysate that is suitable for protein analysis and wherein the protein content of said lysate is representative of the total protein content of said biological sample.

2. (Currently amended) The method according to claim 1, wherein said biological sample comprises a ~~substantially~~ homogeneous population of tissues or cells.

3. (Previously presented) The method according to claim 1, further comprising, prior to step (a), the step of removing any paraffin present in said biological sample by one or more methods selected from the group consisting of: adding an organic solvent; heating; heating and adding a buffer comprising Tris; and heating and adding an organic solvent.

4. (Currently amended) The method according to claim 1, further comprising**, prior to step (b),** the step of mechanically disrupting said biological sample by at least one technique selected from the group consisting of: manual homogenization; vortexing; and physical mixing.

5-8. (Canceled)

9. (Previously presented) The method according to claim 1, wherein said reaction buffer comprises a detergent.

10. (Previously presented) The method according to claim 1, wherein step (b) is carried out in the presence of a detergent.

11. (Currently amended) The method according to claim 9, wherein said detergent is selected from the group consisting of ~~Nonidet P40~~ **NONIDET P40**, SDS, ~~Tween 20~~ **TWEEN 20**, ~~Triton X~~ **TRITON X**, and sodium deoxycholate.

12. (Currently amended) The method according to claim 10, wherein said detergent is selected from the group consisting of ~~Nonidet P40~~ **NONIDET P40**, SDS, ~~Tween 20~~ **TWEEN 20**, ~~Triton X~~ **TRITON X**, and sodium deoxycholate.

13. (Canceled)

14. (Currently amended) The method according to claim 1, wherein said reaction buffer comprises Tris and has a pH in the range of ~~about~~ 1.0 to ~~about~~ 9.0.

15. (Currently amended) A **method of preparing a biomolecule lysate, comprising the steps of:**

(a) heating a composition comprising a formalin fixed biological sample and a reaction buffer at a temperature from 80°C to 100°C for a period of time from 10 minutes to 4 hours to reverse or release protein cross-linking in said biological sample,

(b) treating the resulting composition with an effective amount of a proteolytic enzyme selected from the group consisting of trypsin, chymotrypsin, and endoproteinase Lys-C for a period of time from 30 minutes to 24 hours at a temperature between 37°C to 65°C to disrupt the tissue and cellular structure of said biological sample and to liquefy said sample, thereby producing a liquid, soluble, dilutable biomolecule lysate that

is suitable for protein analysis and wherein the protein content of said lysate is representative of the total protein content of said biological sample, and

~~The method according to claim 1, further comprising the step of~~ fractionating said biomolecule lysate into distinct and separate biomolecule fractions.

16. (Previously presented) The method according to claim 15, wherein each biomolecule fraction contains distinct and separate biomolecules suitable for use in biochemical assays.

17. (Previously presented) The method according to claim 1, wherein said biological sample is selected from a group consisting of formalin-fixed tissue/cells, formalin-fixed/paraffin embedded (FFPE) tissue/cells, FFPE tissue blocks and cells from those blocks, and tissue culture cells that have been formalin fixed and or paraffin embedded.

18-39. (Canceled)

40. (Previously presented) The method of claim 15, wherein said fractionating is carried out using a method selected from the group consisting of step spin column fractionation, immunoprecipitation, gradient centrifugation, HPLC and drip column fractionation.

41. (Previously presented) The method of claim 1, further comprising assaying said biomolecule lysate using mass spectrometry.

42. (New) The method according to claim 1, wherein said reaction buffer comprises Tris and has a pH in the range of 6.0 to 9.0.

Examiner's Reasons for Allowance

8. The closest applicable art to instantly claimed invention are:

- US Patent 5,672,696 issued 30 Sept 1997 to Wang et al. , issued, from IDS dated 29 May 2007). Wang et al. describe a method having steps similar to those claimed instantly. However, the resulting cell lysate is comprised of three distinct visible layers: an insoluble, a soluble and a soluble layer after DNA precipitation in contrast to one soluble liquid, without any distinct visible layers.

- Non-Patent Literature publication by Banerjee et al. 1995. Microwave-e-Based DNA Extraction from Paraffin-embedded tissue for PCR Amplification. Biotechniques, Volume 18, Number 5, Pages 771-773. Banerjee et al. teach a method to obtain a cell lysate prepared from paraffin fixed tissue. The method, however, does not explicitly describes steps of heating, enzyme treatment and cell lysis under the same parameters of temperature, time and pH as instantly claimed. Furthermore, the resultant lysate comprises a soluble and a non-soluble layer, i.e., the lysate is not a clear liquid. Additionally, the number of fractions obtained do not represent the original protein molecule(s).

The claimed invention, however, describes a method having steps elucidating specific temperature, pH and time ranges to treat the paraffin fixed tissue materials to deparrafinnize, change the protein orientating/folding and further the fractionation methods to obtain a cell/tissue lysate that is clear and homogeneous and upon enzymatic treatment releases fractions that are more close representatives of the proteins present in the original sample.. Therefore, the claimed invention is neither anticipated by, nor is obvious over the cited prior art referred to *supra*.

9. Any comments considered necessary by applicants must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Conclusion

10. Claims 1-4, 9-12, 14-17 and 40-42 are allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Kailash C. Srivastava whose telephone number is (571) 272-0923. The examiner can normally be reached on Monday to Thursday from 7:30 A.M. to 6:00 P.M. (Eastern Standard or Daylight Savings Time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Jon Weber can be reached at (571)-272-0925 Monday through Thursday 7:30 A.M. to 6:00 P.M. The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding may be obtained from the Patent Application Information Retrieval (i.e., PAIR) system. Status information for the published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (i.e., EBC) at: (866)-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Dr. Kailash C Srivastava/
Examiner, Art Unit 1657

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12 November 2008

/JON P WEBER/
Supervisory Patent Examiner, Art Unit 1657